Supplementary appendix

Automatic analysis of bronchus-artery dimensions to diagnose and monitor airways disease in cystic fibrosis

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S1: LungQ Algorithm to Quantify BA-ratios

LungQ is an AI-based medical image analysis platform that automatically identifies patient-specific anatomical features, structural abnormalities, and diseases from chest CT scans. The image analysis methods implemented in LungQ have been commercially developed and scientifically validated for over eight years. This resulted in several CE and TGA-certified, and FDA-cleared incremental releases of LungQ allowing a wide use in the field. Because of the incremental nature of the platform, new algorithms are built on top of already existing modules to further enhance the clinical value of LungQ. This means that not just a single dataset can be attributed to the development of LungQ, but instead, a wide range of CTs was used to develop and train the algorithms to ensure robust performance against variation in disease populations, such as patients with CF, and variation in image characteristics like kernels and dose. In the full development history of LungQ, multi-centric datasets of inspiratory and expiratory CTs were used including (but not limited to) CT coming from a variety in patient characteristics (such as age, gender, BMI), scanner characteristics (such as manufacturer, dose, convolutional kernel, voxel spacing), and diseases (such as COPD, Asthma, CF, ILD, chronic bronchitis, bronchiectasis, COVID-19). For each AI-based model, specific manual annotations were created to train the models to perform a certain task. These annotations (or training samples) were manually created by expert data analysts, trained within Thirona's ISO 13485 certified image analysis service. Because of this process, AI-based algorithms in LungQ have been trained using thousands of CT scans from which millions of training samples were created to train each model for a specific task.

Supplementary Tables

Table S1. Difference between the manual and automatic BA-analysis in B_{out}/A, B_{in}/A, and B_{wt}/A from G_1 to G_5 of CF-control dataset

B_{out}/A			
	Value	Standard error	P-value
(Intercept)	0.042	0.081	0.607
Method (manual BA-analysis)	-0.005	0.005	0.277
Disease (control)	-0.148	0.041	0.002
Age	0.022	0.010	0.034
Gender (male)	-0.052	0.041	0.222
Total lung volume	$-3.56*e-^{5}$	$2.10*e^{-5}$	0.090
B_{in}/A			
	Value	Standard error	P-value
(Intercept)	-0.527	0.275	0.055
Method (manual BA-analysis)	-0.414	0.005	<0.001*
Disease (control)	-0.104	0.139	0.465
Age	0.131	0.026	<0.001
Gender (male)	-0.091	0.140	0.521
Total lung volume	-0.0003	$2.53*e^{-5}$	<0.001
B_{wt}/A			
	Value	Standard error	P-value
(Intercept)	-1.624	0.315	<0.001
Method (manual BA-analysis)	0.613	0.007	<0.001*
Disease (control)	-0.226	0.159	0.172
Age	-0.130	0.030	<0.001
Gender (male)	-0.022	0.160	0.894
Total lung volume	0.0004	$4.31*e^{-5}$	<0.001

BA-analysis: bronchus-artery analysis; B_{out}/A ratio: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A ratio: the ratio between the bronchial wall thickness and artery diameter; G: segmental generation. *: p-value less than 0.05 is considered a significant difference between manual and automatic BA-analysis.

Note that the models have log-transformed response and the coefficient (value) and standard error are presented on log-scale.

Table S2. Delong test of discriminating ability between the manual and automatic BA-analysis in B_{out}/A ratio results from G_1 to G_5

Segmental generation		**G_1**	**G_2**	**G_3**	**G_4**	**G_5**
AUC	*Manu.*	0.67	0.83	0.80	0.87	0.84
(95% CI)		(0.44-0.91)	(0.64 - 1)	(0.59 - 1)	(0.71 - 1)	(0.66 - 1)
	Auto.	0.67	0.72	0.83	0.89	0.94
		(0.45-0.90)	(0.50-0.93)	(0.66-0.99)	(0.76 - 1)	(0.81 - 1)
P-value		0.99	0.42	0.82	0.83	0.38

BA-analysis: bronchus-artery analysis; B_{out}/A ratio: the ratio of bronchial outer diameter and adjacent artery diameter; G: segmental generation, G_1 is sub-segmental bronchi; AUC: area under the curve; 95% CI: 95% confidence interval; Manu.: the manual BA-analysis; Auto.: the automatic BA-analysis analysis. A p-value less than 0.05 is considered a significant difference.

Table S3. Delong test of discriminating ability between the manual and automatic BA-analysis in B_{in}/A ratio results from G_1 to G_5

Segmental generation		**G_1**	**G_2**	**G_3**	**G_4**	**G_5**
AUC	*Manu.*	0.56	0.66	0.62	0.63	0.70
(95% CI)		(0.31-0.81)	(0.42-0.89)	(0.38-0.86)	(0.39-0.87)	(0.46-0.94)
	Auto.	0.47	0.47	0.58	0.64	0.81
		(0.22-0.72)	(0.22-0.72)	(0.33-0.83)	(0.41-0.88)	(0.62 - 1)
P-value		0.61	0.27	0.80	0.93	0.47

BA-analysis: bronchus-artery analysis; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter; G: segmental generation, G_1 is sub-segmental bronchi; AUC: area under the curve; 95%

CI: 95% confidence interval; Manu.: the manual BA-analysis; Auto.: the automatic BA-analysis. A p-value less than 0.05 is considered a significant difference.

Table S4. Delong test of discriminating ability between the manual and automatic BA-analysis in B_{wt}/A ratio results from G_1 to G_5

Segmental generation		**G_1**	**G_2**	**G_3**	**G_4**	**G_5**
AUC	*Manu.*	0.80	0.80	0.80	0.85	0.79
(95% CI)		(0.60-0.99)	(0.62-0.99)	(0.61-0.99)	(0.68 - 1)	(0.57 - 1)
	Auto.	0.81	0.83	0.85	0.91	0.94
		(0.64-0.99)	(0.65 - 1)	(0.68 - 1)	(0.79 - 1)	(0.85 - 1)
P-value		0.90	0.86	0.73	0.58	0.23

BA-analysis: bronchus-artery analysis; B_{wt}/A ratio: the ratio between bronchial wall thickness and adjacent artery diameter; G: segmental generation, G_1 is sub-segmental bronchi; AUC: area under the curve; 95% CI: 95% confidence interval; Manu.: the manual BA-analysis; Auto.: the automatic BA-analysis. A p-value less than 0.05 is considered a significant difference.

Table S5-1. Threshold of BA-ratios calculated by Youden test based on the results of the CF-control dataset assessed by the automatic BA-analysis

BA-ratios	Segmental generation						
	G1	G2	G3	G4	G5	Median	Mean
B_{out}/A	1.24	0.97	1.05	1.03	0.99	1.03*	1.02*
B_{in}/A	0.67	0.70	0.65	0.63	0.79	0.66*	0.68*
B_{wt}/A	0.16	0.15	0.12	0.13	0.11	0.13*	0.13*

Table S5-2. The 95% confidence interval of BA-ratios in control subjects of CF-control dataset assessed by the automatic BA-analysis

BA-ratios	95% Confidence Interval		
	2.5 percentile	mean	97.5 percentile
B_{out}/A	1.06	1.07	1.09#
B_{in}/A	0.78	0.79	0.81#
B_{wt}/A	0.14	0.14	0.14#

BA: bronchus-artery; G: segmental generation, G_1 is sub-segmental bronchi; B_{out}/A ratio: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A ratio: the ratio between bronchial wall thickness and adjacent artery diameter.

Note: In our approach, we have tried to find the best cut-off value that discriminates CF from control subjects by using Youden test to capture the performance of a dichotomous diagnostic test. We also calculated the 95% confidence interval of BA-ratios in control subjects of CF-control dataset as there were normal BA-pairs in the lung of CF patients which may reduce the threshold obtained by Youden test. In above calculation (table S5-1, S5-2), we compared the median and mean of threshold (the value with * in table S5-1) and the 97.5 percentile (upper level of 95% CI) (the value with # in table S5-2) in BA-ratios to investigate the applicable cut-off value of BA-ratios to diagnose bronchial widening and wall thickening based on measurements of the CF-control dataset. As the results of these two methods (the value with * in table S5-1 and the value with # in table S5-2) give very similar thresholds, we determined that the optimal cut-off values to define bronchial widening: for B_{out}/A ratio is 1.1 and for B_{in}/A ratio is 0.8. The optimal cut-off of B_{wt}/A ratio to define bronchial wall thickening is 0.14.

Table S6. The change in B_{out}/A, B_{in}/A, and B_{wt}/A ratios results in generations G_1-G_5 and all generations (G_1-G_{12})-sensitivity analysis over 2 years interval of the Copenhagen dataset

	Limited generations (G_1-G_5)			**Sensitivity analysis (G_1-G_{12})**		
B_{out}/A						
	Value	Standard Error	P-value	value	Standard Error	P-value
Intercept	0.865	0.102	<0.001	0.866	0.105	<0.001
State (baseline)	0.009	0.002	<0.001*	0.008	0.002	<0.001*
Baseline age	-0.001	0.005	0.863	-0.001	0.006	0.856
Baseline height	0.002	0.001	0.159	0.001	0.001	0.192
Gender (male)	-0.019	0.014	0.181	-0.019	0.015	0.201
Total lung volume	$-5.28*e^{-6}$	$2.94*e^{-6}$	0.073	$-2.24*e^{-6}$	$2.86*e^{-6}$	0.434
B_{in}/A						
	Value	Standard Error	P-value	value	Standard Error	P-value
Intercept	0.707	0.085	<0.001	0.704	0.088	<0.001
State (baseline)	0.008	0.002	<0.001*	0.008	0.002	<0.001*
Baseline age	-0.003	0.005	0.487	-0.003	0.005	0.498
Baseline height	0.002	0.001	0.098	0.002	0.001	0.113
Gender (male)	-0.0002	0.012	0.983	0.001	0.012	0.947
Total lung volume	$-1.30*e^{-6}$	$2.51*e^{-6}$	0.606	$9.54*e^{-6}$	$2.46*e^{-6}$	0.698
B_{wt}/A						
	Value	Standard Error	P-value	value	Standard Error	P-value
Intercept	0.338	0.077	<0.001	0.345	0.077	<0.001
State (baseline)	0.002	0.001	0.025[#]	0.002	0.001	0.077
Baseline age	0.002	0.004	0.659	0.002	0.004	0.688
Baseline height	0.0004	0.001	0.595	0.0004	0.001	0.654
Gender (male)	-0.025	0.011	0.025	-0.027	0.011	0.019
Total lung volume	$-5.61*e^{-6}$	$1.66*e^{-6}$	<0.001	$-4.20*e^{-6}$	$1.61*e^{-6}$	0.009

B_{out}/A ratio: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A ratio: the ratio of bronchial wall thickness and adjacent artery diameter; G: segmental generation, G_1 is sub-segmental bronchi. *: A p value less than 0.05 indicates a significant difference. Note that limited generations included 89% BA-pairs relative to the BA-pairs in all generations.

Note that the models have log-transformed response and the coefficient (value) and standard error are presented on log-scale. [#]: The p value from the model with limited generations (p=0.025) is very close to 0.05 and quite similar as the p value from the model with all generations (p=0.077). According to the coefficient of the model for B_{wt}/A outcome and the effect plots (figure S12, S13), we prefer to focus on the clinically relevant not the statistically significant. So, we identified no progression in B_{wt}/A outcome detected over 2 years intervals in Copenhagen dataset.

Table S7. The change in B_{out}/A, B_{in}/A, and B_{wt}/A ratios results in generations G_1-G_6 and all generations (G_1-G_{15})-sensitivity analysis over 48 weeks interval of the ataluren dataset

	Limited generations(G_1-G_6)			**Sensitivity analysis(G_1-G_{15})**			**G_1-G_5**		
B_{out}/A									
	Value	Std. Error	P-value	Value	Std. Error	P-value	Value	Std. Error	P-value
Intercept	1.198	0.080	<0.001	1.181	0.081	<0.001	1.202	0.080	<0.001
State (baseline)	0.008	0.001	<0.001	0.008	0.001	<0.001	0.008	0.001	<0.001
Baseline age	0.001	0.001	0.257	0.001	0.001	0.261	0.001	0.001	0.247
Gender (male)	-0.026	0.012	0.033	-0.027	0.012	0.025	-0.024	0.012	0.046
Baseline height	-0.001	0.001	0.228	-0.001	0.001	0.366	-0.001	0.001	0.190
Total lung volume	$2.88*e^{-6}$	$2.19*e^{-6}$	<0.001	$2.83*e^{-6}$	$2.16*e^{-6}$	<0.001	$2.91*e^{-6}$	$2.22*e^{-6}$	<0.001
B_{in}/A									
	Value	Std. Error	P-value	Value	Std. Error	P-value	Value	Std. Error	P-value
Intercept	0.078	0.155	0.615	0.040	0.154	0.794	0.090	0.156	0.563
State (baseline)	0.014	0.002	<0.001	0.014	0.001	<0.001	0.014	0.002	<0.001
Baseline age	0.0001	0.001	0.917	0.0002	0.001	0.829	$3.65*e^{-6}$	0.001	0.976
Gender (male)	-0.079	0.023	<0.001	-0.078	0.023	<0.001	-0.078	0.023	<0.001
Baseline height	-0.003	0.001	0.007	-0.003	0.001	0.017	-0.003	0.001	0.004
Total lung volume	$8.89*e^{-6}$	$3.82*e^{-6}$	<0.001	$8.65*e^{-6}$	$3.76*e^{-6}$	<0.001	$9.06*e^{-6}$	$3.90*e^{-6}$	<0.001
B_{wt}/A									
	Value	Std. Error	P-value	Value	Std. Error	P-value	value	Std. Error	P-value
Intercept	0.398	0.046	<0.001	0.401	0.044	<0.001	0.397	0.046	<0.001
State (baseline)	0.003	0.001	<0.001	0.003	0.0004	<0.001	0.003	0.001	<0.001
Baseline age	0.0004	0.0003	0.237	0.001	0.0003	0.074	0.001	0.0004	0.142
Gender (male)	0.009	0.007	0.186	0.007	0.007	0.296	0.011	0.007	0.112
Baseline height	0.001	0.0003	0.031	0.001	0.0003	0.028	0.001	0.0003	0.036
Total lung volume	$-8.06*e^{-6}$	$1.20*e^{-6}$	<0.001	$-8.28*e^{-6}$	$1.11*e^{-6}$	<0.001	$-7.85*e^{-6}$	$1.23*e^{-6}$	<0.001

B_{out}/A ratio: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A ratio: the ratio of bronchial wall thickness and adjacent artery diameter; G: segmental generation, G_1 is sub-segmental bronchi; Std.Error: standard error. Note that limited generations included 90% BA-pairs relative to the BA-pairs in all generations. P value less than 0.05 indicates a significant difference.

Note that the models of B_{out}/A and B_{wt}/A have square root-transformed response and the model of B_{in}/A has log-transformed response. The coefficient (value) and standard error (Std.Error) are presented on sqrt-scale or log-scale.

Table S8. The results of PRAGMA-CF on structure lung disease and pulmonary function tests in two longitudinal datasets(1-3)

PRAGMA-CF	**Copenhagen dataset**			**ataluren dataset**		
Mean[range]	Baseline	Follow-up	Mean difference	Baseline	Follow up	Mean difference
%BE	2.3 [0.7-4.7]	2.1 [0.7-5.7]	0.3 (p = 0.4)	7.8 [0-35.3]	8.9 [0-48.6]	1.07 (p=0.08)
%Disease	5.0 [3.0-9.7]	4.1 [2.1-9.9)	−0.5 (p = 0.3)	10.0 [0-35.4]	11.2 [0-52.3]	1.23 (p=0.008*)
Pulmonary function test Median (range)						
FVC%pred	98 (91-108)			78 (57–109)		

PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; %Disease: percentage of lung volume occupied by abnormal airways; FVC%pred: forced vital capacity as percent of predicted value. * P value less than 0.05 means significant difference.

Table S9. The change in diameter of the arteries for each BA-pair over two years interval of the Copenhagen dataset in generations G_1-G_5

Mixed effected models	**Limited generations**		
	G_1-G_5		
	Estimate	Std. Error	P-value
Paired Artery	-0.002	0.001	0.10

BA-pair: bronchus-artery pair; G: segmental generation, G_1 is sub-segmental bronchi; Std. Error: standard error. P value less than 0.05 indicates a significant difference.

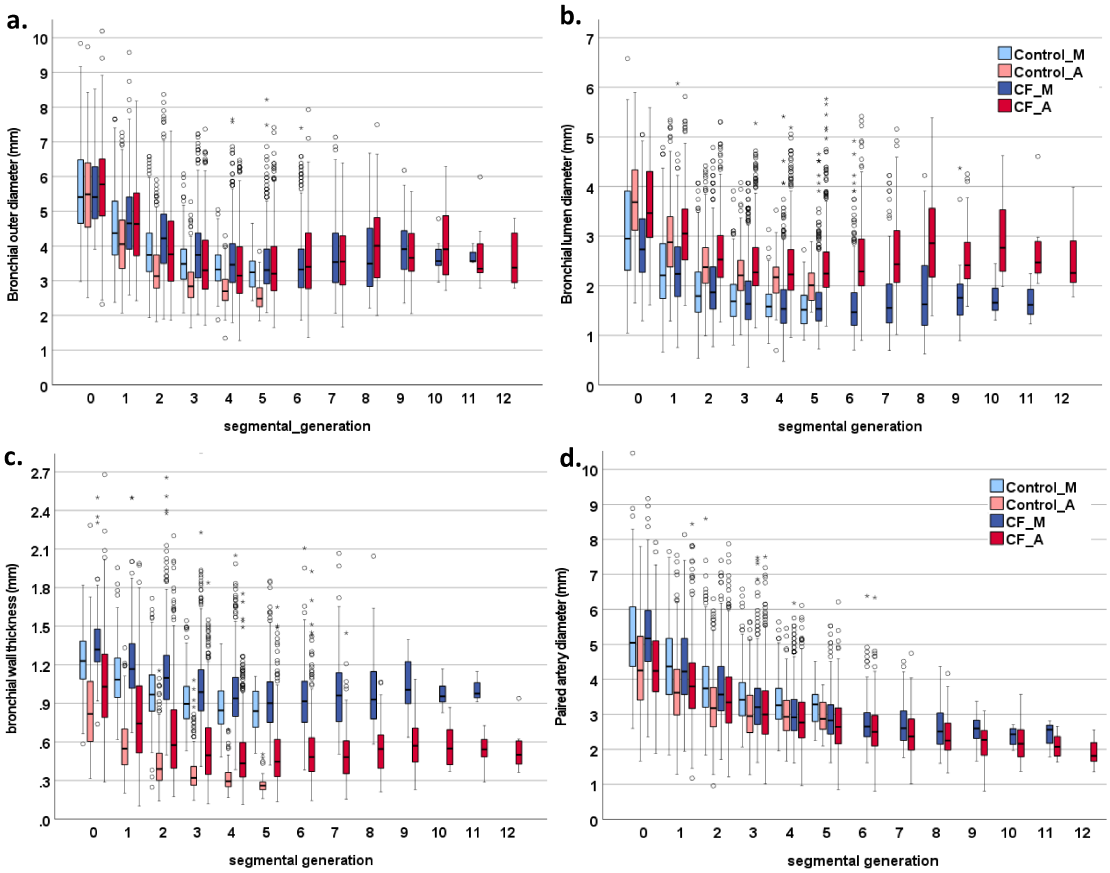
Table S10. The change in diameter of arteries for each BA-pair over 48 weeks interval of the ataluren dataset in generations G_1-G_6

Mixed effected models	**Limited generations**		
	G_1-G_6		
	Estimate	Std. Error	P-value
Paired Artery	-0.0003	0.001	0.83

BA-pair: bronchus-artery pair; G: segmental generation, G_1 is sub-segmental bronchi; Std. Error: standard error. P value less than 0.05 indicates significant difference.

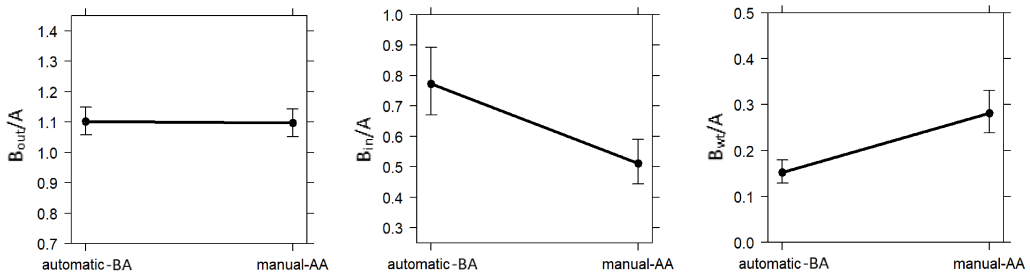
Supplementary Figures

Figure S1. Boxplots of the dimensions of bronchus-artery (BA) pairs assessed by manual and automatic BA-analysis for each segmental generation of CF-control dataset



Control_M: control subjects assessed by the manual method (light blue); Control_A: the control subjects assessed by automatic BA-analysis (pink); CF_M: the subjects with cystic fibrosis assessed by manual method (dark blue); CF_A: the subjects with cystic fibrosis assessed by automatic BA-analysis (red). Note that 0 in the horizontal axis is the segmental bronchi and 1 for sub-segmental bronchi. Each box shows median (horizontal line), interquartile range (solid box), 1.5*quartile range (whiskers), and outliers (circle and asterisk). a. boxplot of the bronchial outer diameter in each segmental generation, b. boxplot of the bronchial lumen diameter, c. boxplot of bronchial wall thickness, and d. boxplot of the adjacent artery. The unit of vertical axis is in millimeter.

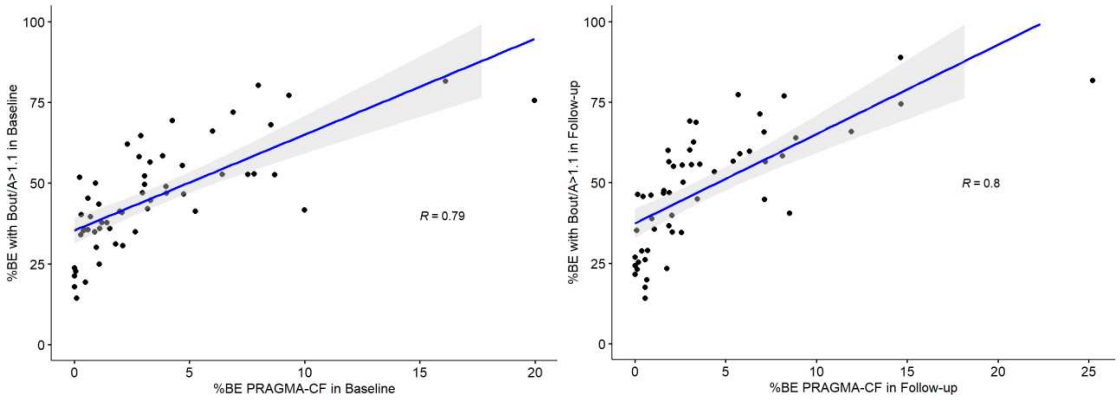
Figure S2. Difference between manual and automatic BA-analysis in BA-ratios from G_1 to G_5 in the CF-control dataset



BA: bronchial-artery; G: segmental generation, G_1 indicates sub-segmental bronchi; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A: the ratio between bronchial wall thickness and adjacent artery diameter; automatic-BA: the automaitc BA-analysis; manual-BA: the manual Bronchus-Artery analysis.

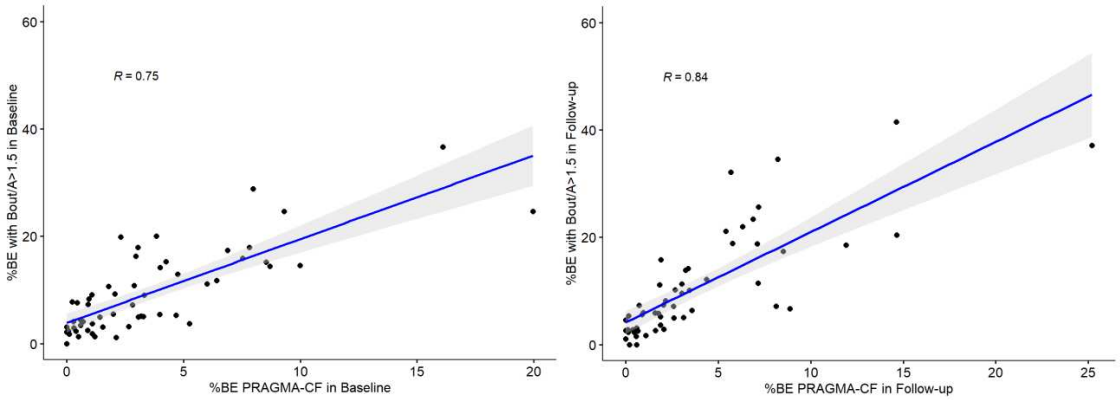
Mean predicted (95% confidence interval, 95%CI) values of B_{out}/A, B_{in}/A, and B_{wt}/A in G_1-G_5 were estimated from mixed-effects model. Predicted BA-ratios are the estimated outcomes when assuming specific values (mean or mode) for other variables. For B_{out}/A, the mean predicted values in G_1-G_5 are 1.102 (95%CI 1.057 to 1.149) of automatic BA-analysis and 1.097 (95%CI 1.052 to 1.143) of manual BA-analysis (p=0.277). For B_{in}/A, the mean predicted values in G_1-G_5 is 0.77 (95%CI 0.671 to 0.892) of automatic BA-analysis and 0.51 (95%CI 0.443 to 0.590) of manual BA-analysis (p<0.001). For B_{wt}/A, the mean predicted values in G_1-G_5 is 0.15 (95%CI 0.129 to 0.179) of automatic BA-analysis and 0.28 (95%CI 0.239 to 0.331) of manual BA-analysis (p<0.001).

Figure S3. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{out}/A >1.1) at baseline and follow-up in the Copenhagen dataset



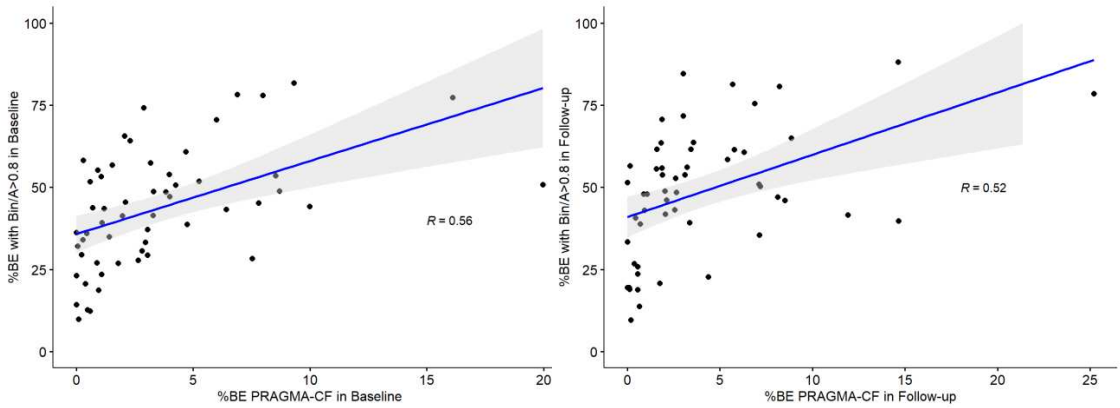
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter.

Figure S4. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{out}/A >1.5) at baseline and follow-up in the Copenhagen dataset



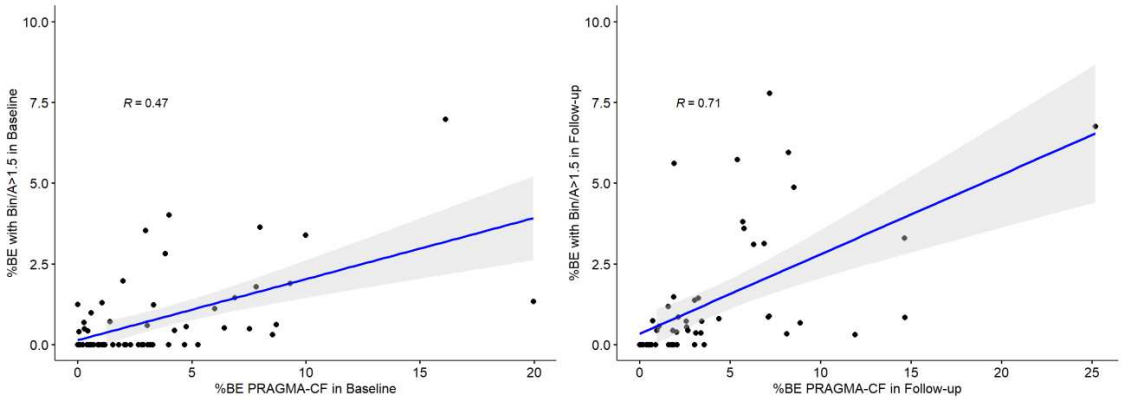
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter.

Figure S5. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{in}/A >0. 8) at baseline and follow-up in the Copenhagen dataset



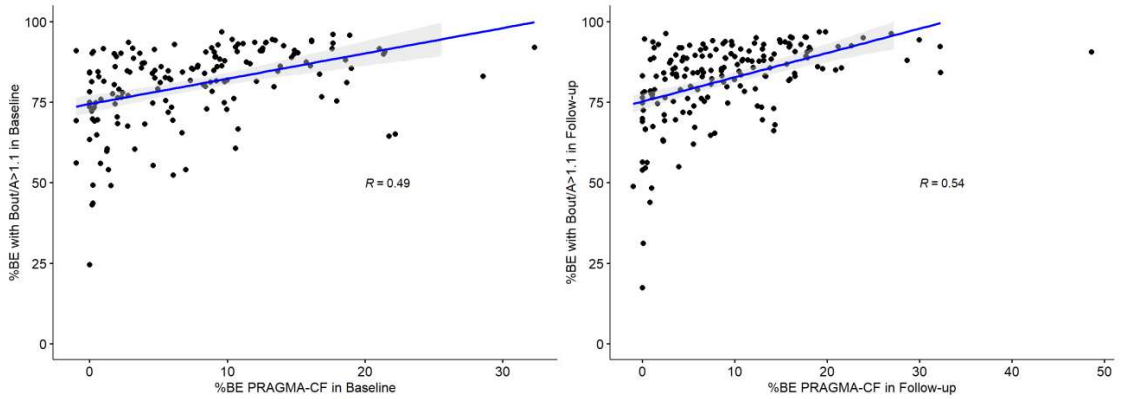
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter.

Figure S6. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{in}/A >1.5) at baseline and follow-up in the Copenhagen dataset



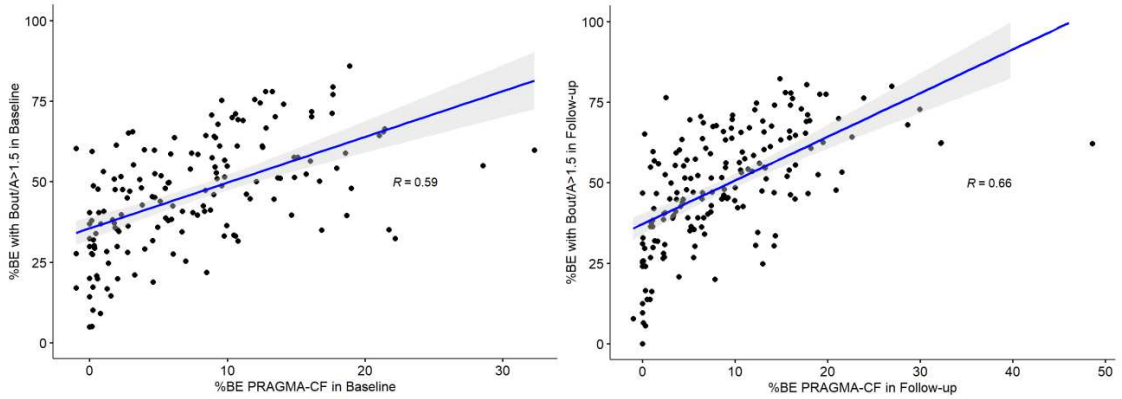
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter.

Figure S7. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{out}/A >1.1) at baseline and follow-up in the ataluren dataset



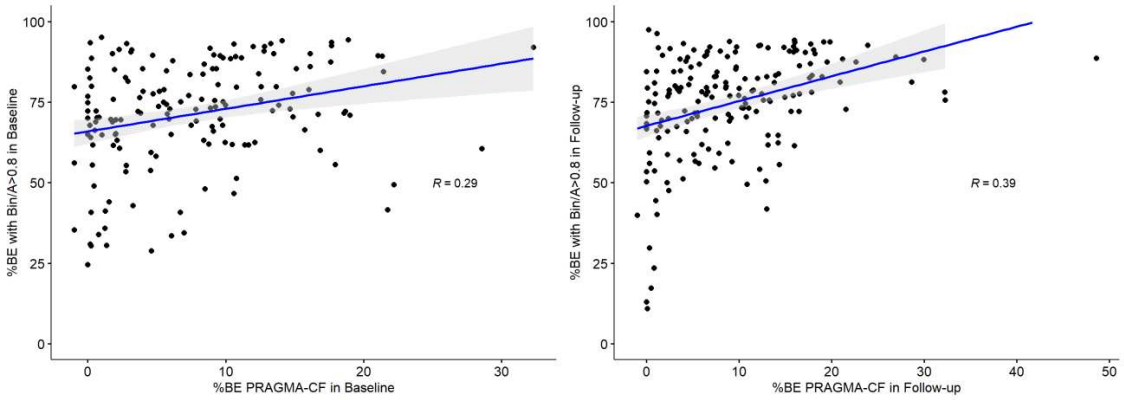
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter.

Figure S8. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{out}/A >1.5) at baseline and follow-up in the ataluren dataset



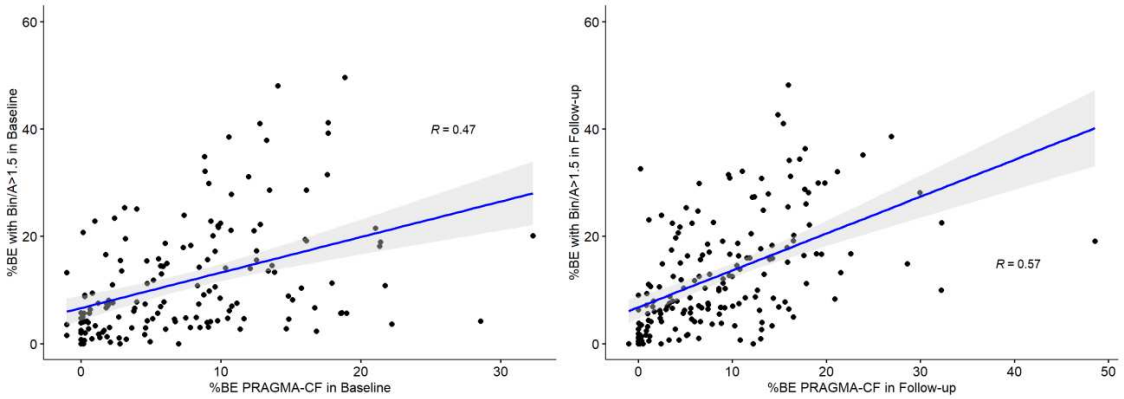
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter.

Figure S9. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{in}/A >0.8) at baseline and follow-up in the ataluren dataset



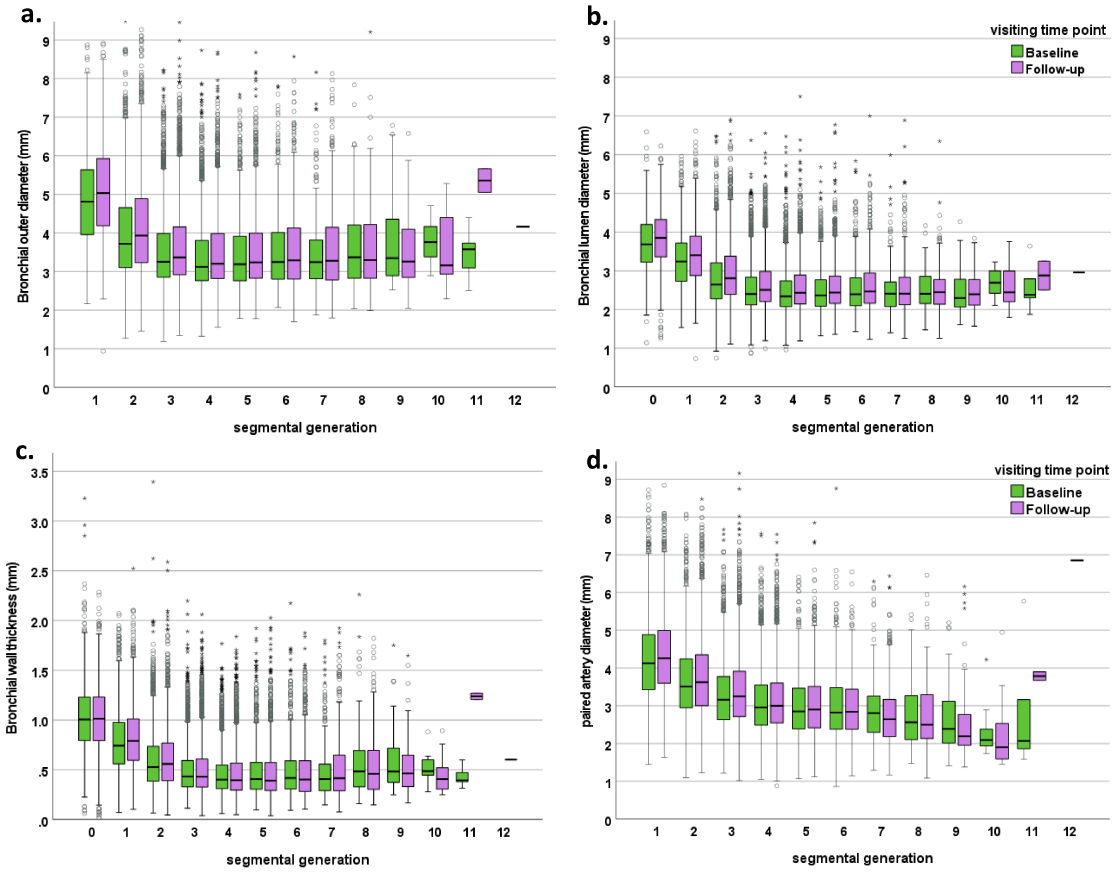
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter.

Figure S10. The correlation between manual PRAGMA-CF %Bronchiectasis (%BE) and the automatic BA-analysis %BE (B_{in}/A >1.5) at baseline and follow-up in the ataluren dataset



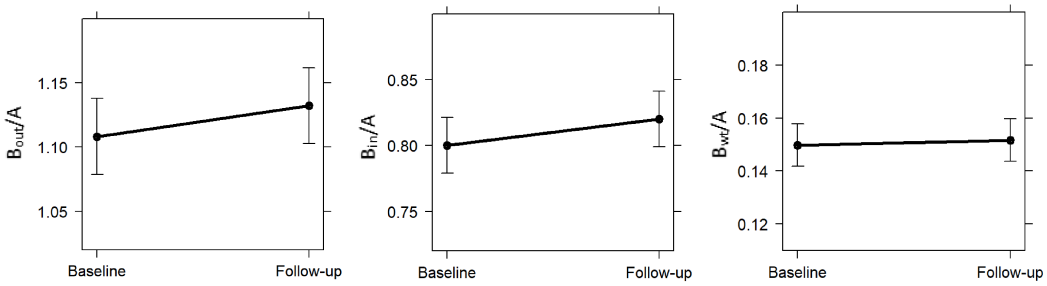
PRAGMA-CF: The Perth-Rotterdam Annotated Grid Morphometric Analysis for Cystic Fibrosis; %BE: percentage of bronchiectasis in inspiratory scan; B_{in}/A ratio: the ratio of bronchial lumen diameter and adjacent artery diameter.

Figure S11. Boxplots of the dimensions of bronchial-artery pairs at baseline (green) and at follow-up (purple) for each segmental generation of Copenhagen dataset



Note that 0 in the horizontal axis are the segmental bronchi and 1 for sub-segmental bronchi. Each box shows median (horizontal line), interquartile range (solid box), 1.5*quartile range (whiskers), and outliers (circle and asterisk). **a.** boxplot of the bronchial outer diameter in each segmental generation, **b.** boxplot of the bronchial lumen diameter, **c.** boxplot of bronchial wall thickness, and **d.** boxplot of the adjacent artery in each segmental generation. The unit of vertical axis is in millimeter.

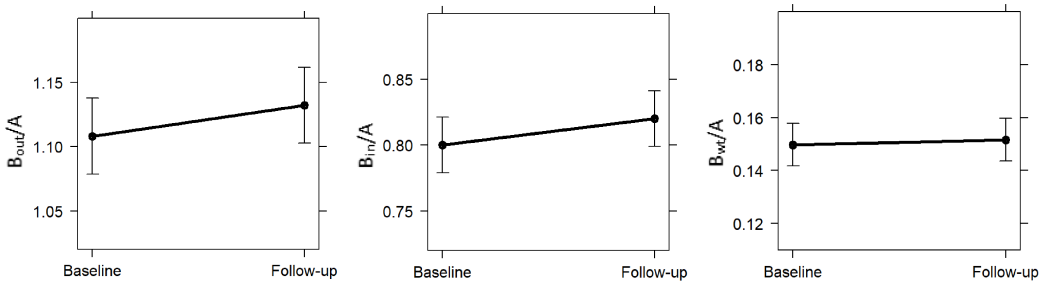
Figure S12. Change from baseline to follow-up in BA-ratios in generations G_1-G_5 in the Copenhagen dataset



BA: bronchus-artery; G: segmental generation, G_1 indicates sub-segmental bronchi; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A: the ratio of bronchial wall thickness and adjacent artery diameter.

Mean predicted (95% confidence interval, 95%CI) values of B_{out}/A, B_{in}/A, and B_{wt}/A in G_1-G_5 were estimated from mixed-effects model. Predicted BA-ratios are the estimated outcomes when assuming specific values (mean or mode) for other variables. For B_{out}/A, the mean predicted values in G_1-G_5 are 1.10 (95%CI 1.070 to 1.127) at baseline and 1.12 (95%CI 1.096 to 1.153) at follow-up ($p<0.001$). For B_{in}/A, the mean predicted values in G_1-G_5 are 0.79 (95%CI 0.771 to 0.811) at baseline and 0.81 (95%CI 0.792 to 0.832) at follow-up ($p<0.001$). For B_{wt}/A, the mean predicted values in G_1-G_5 are 0.150 (95%CI 0.142 to 0.158) at baseline and 0.152 (95%CI 0.144 to 0.160) at follow-up ($p=0.025$).

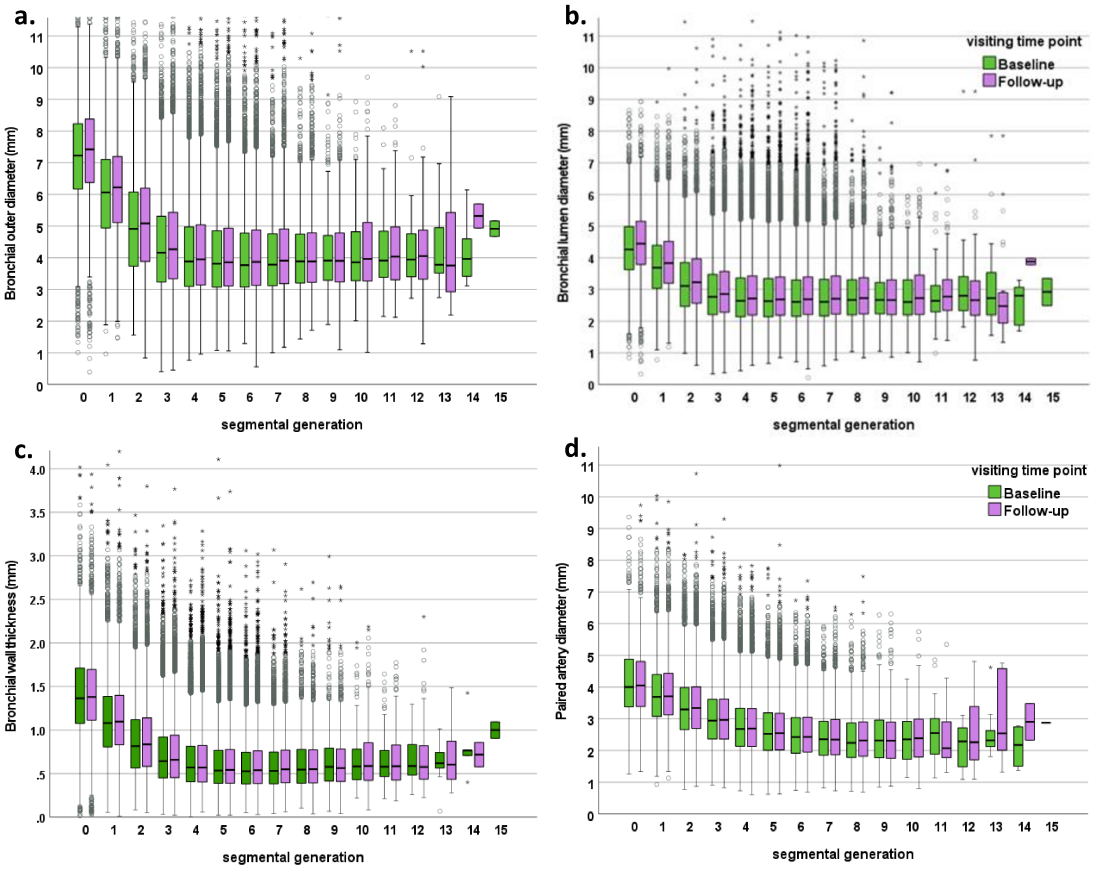
Figure S13. Change from baseline to follow-up in BA-ratios in all generations G_1-G_{12} in the Copenhagen dataset – sensitivity analysis



BA: bronchial-artery; G: segmental generation, G_1 indicates sub-segmental bronchi; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A: the ratio of bronchial wall thickness and adjacent artery diameter.

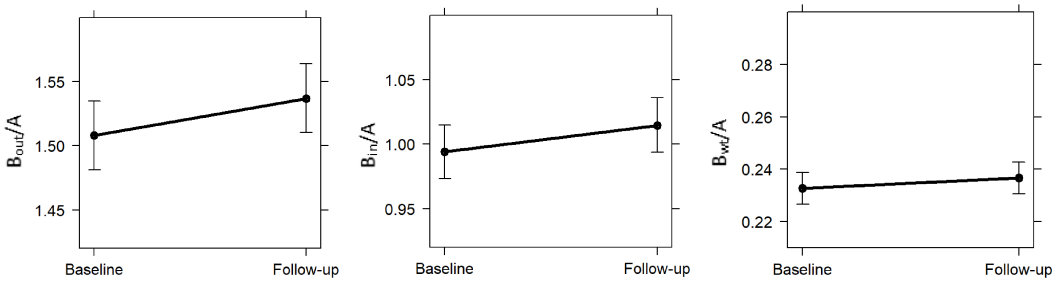
Mean predicted (95% confidence interval, 95%CI) values of B_{out}/A, B_{in}/A, and B_{wt}/A in all generations were estimated from mixed-effects model. Predicted BA-ratios are the estimated outcomes when assuming specific values (mean or mode) for other variables. For B_{out}/A, the mean predicted values in G_1-G_{12} are 1.11 (95%CI 1.079 to 1.138) at baseline and 1.13 (95%CI 1.103 to 1.162) at follow-up ($p<0.001$). For B_{in}/A, the mean predicted values in G_1-G_{12} are 0.80 (95%CI 0.779 to 0.821) at baseline and 0.82 (95%CI 0.799 to 0.841) at follow-up ($p<0.001$). For B_{wt}/A, the mean predicted values in G_1-G_{12} are 0.150 (95%CI 0.142 to 0.158) at baseline and 0.152 (95%CI 0.144 to 0.160) at follow-up ($p=0.077$).

Figure S14. Boxplots of the dimensions of bronchus-artery pairs at baseline (green) and at follow-up (purple) for each segmental generation of ataluren study



Note that 0 in the horizontal axis is the segmental bronchi and 1 is for sub-segmental bronchi. Each box shows median (horizontal line), interquartile range (solid box), 1.5*quartile range (whiskers), and outliers (circle and asterisk). **a.** boxplot of the bronchial outer diameter in each segmental generation, **b.** boxplot of the bronchial lumen diameter, **c.** boxplot of bronchial wall thickness, and **d.** boxplot of the adjacent artery in each segmental generation. The unit of vertical axis is in millimeter.

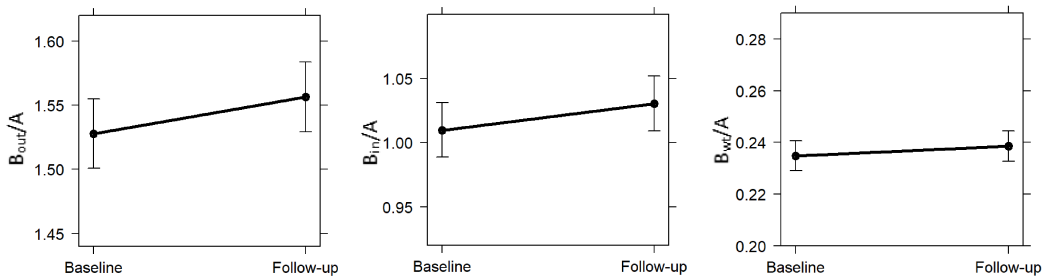
Figure S15. Change from baseline to follow-up in BA-ratios in generations G_1-G_6 in the ataluren dataset



BA: bronchus-artery; G: segmental generation, G_1 indicates sub-segmental bronchi; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A: the ratio of bronchial wall thickness and adjacent artery diameter.

Mean predicted (95% confidence interval, 95%CI) values of B_{out}/A, B_{in}/A, and B_{wt}/A in G_1-G_6 were estimated from mixed-effects model. Predicted BA-ratios are the estimated outcomes when assuming specific values (mean or mode) for other variables. For B_{out}/A, the mean predicted values in G_1-G_6 are 1.51 (95%CI 1.481 to 1.535) at baseline and 1.54 (95%CI 1.510 to 1.564) at follow-up ($p<0.001$). For B_{in}/A, the mean predicted values in G_1-G_6 are 0.99 (95%CI 0.973 to 1.015) at baseline and 1.01 (95%CI 0.994 to 1.036) at follow-up ($p<0.001$). For B_{wt}/A, the mean predicted values in G_1-G_6 are 0.23 (95%CI 0.227 to 0.239) at baseline and 0.24 (95%CI 0.231 to 0.243) at follow-up ($p<0.001$).

Figure S16. Change from baseline to follow-up in BA-ratios in all generations G_1-G_{15} in the ataluren dataset – sensitivity analysis



BA: bronchus-artery; G: segmental generation, G_1 indicates sub-segmental bronchi; B_{out}/A: the ratio of bronchial outer diameter and adjacent artery diameter; B_{in}/A: the ratio of bronchial lumen diameter and adjacent artery diameter; B_{wt}/A: the ratio of bronchial wall thickness and adjacent artery diameter.

Mean predicted (95% confidence interval, 95%CI) values of B_{out}/A, B_{in}/A, and B_{wt}/A in all generations were estimated from mixed-effects model. Predicted BA-ratios are the estimated outcomes when assuming specific values (mean or mode) for other variables. For B_{out}/A, the mean predicted values in G_1-G_{15} are 1.53 (95%CI 1.501 to 1.555) at baseline and 1.56 (95%CI 1.529 to 1.584) at follow-up ($p<0.001$). For B_{in}/A, the mean predicted values in G_1-G_{15} are 1.01 (95%CI 0.989 to 1.031) at baseline and 1.03 (95%CI 1.009 to 1.052) at follow-up ($p<0.001$). For B_{wt}/A, the mean predicted values in G_1-G_{15} are 0.23 (95%CI 0.229 to 0.241) at baseline and 0.24 (95%CI 0.233 to 0.244) at follow-up ($p<0.001$).

Reference

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